FEP 8.01.49 Intensity-Modulated Radiotherapy for Abdomen and Pelvis

Effective Date: October 15, 2018

Related Policies:
8.01.48 Intensity-Modulated Radiotherapy: Cancer of the Thyroid
8.01.59 Intensity-Modulated Radiotherapy: Central Nervous System Tumors

Intensity-Modulated Radiotherapy for Abdomen and Pelvis

Description
Radiotherapy may be an integral component of the treatment of cancers of the abdomen and pelvis. Intensity-modulated radiotherapy (IMRT) has been proposed as a method that allows adequate radiation to the tumor while minimizing the radiation dose to surrounding normal tissues and critical structures.

Intensity-modulated radiotherapy (IMRT) uses computer software and CT and magnetic resonance images, to offer better conformality than 3D-CRT, because it modulates the intensity of the overlapping radiation beams projected on the target and uses multiple shaped treatment fields. Treatment planning and delivery are more complex, time-consuming, and labor intensive for IMRT than for 3D-CRT. The technique uses a multileaf collimator (MLC), which, when coupled with a computer algorithm, allows for “inverse” treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target’s prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose limits within the normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan’s goals.

Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and thus may improve local tumor control, with decreased exposure to surrounding, normal tissues, potentially reducing acute and late radiation toxicities. Better dose homogeneity within the target may also improve local tumor control by avoiding underdosing within the tumor and may decrease toxicity by avoiding overdosing.

Technologic development has produced advanced techniques that may further improve RT treatment by improving dose distribution. These techniques are considered variations of IMRT. Volumetric modulated arc therapy delivers radiation from a continuous rotation of the radiation source. The principal advantage of volumetric modulated arc therapy is greater efficiency in treatment delivery time, reducing radiation exposure and improving target radiation delivery due to less patient motion. Image-guided RT involves the incorporation of imaging before and/or during treatment to more precisely deliver RT to the target volume.

IMRT methods to plan and deliver RT are not uniform. IMRT may use beams that remain on as MLCs move around the patient (dynamic MLC) or that are off during movement and turn on once the MLC
reaches prespecified positions (“step and shoot” technique). A third alternative uses a very narrow single beam that moves spirally around the patient (tomotherapy). Each method uses different computer algorithms to plan treatment and yields somewhat different dose distributions in and outside the target. Patient position can alter target shape and thus affect treatment plans. Treatment plans are usually based on a single imaging scan, a static 3D-CT image. Current methods seek to reduce positional uncertainty for tumors and adjacent normal tissues by various techniques. Patient immobilization cradles and skin or bony markers are used to minimize day-to-day variability in patient positioning. In addition, many tumors have irregular edges that preclude drawing tight margins on CT scan slices when radiation oncologists contour the tumor volume. It is unknown whether omitting some tumor cells or including some normal cells in the resulting target affects outcomes of IMRT.

**OBJECTIVE**

The objective of this evidence review is to evaluate whether intensity-modulated radiotherapy improves the net health outcome when used to treat cancers of the abdomen and pelvis. Note that the evidence for the following abdominal and pelvic cancers has not yet been reviewed and is beyond the scope of this review: bladder, kidney, ureter, and esophageal cancer and sarcoma.

**POLICY STATEMENT**

Intensity-modulated radiotherapy may be considered *medically necessary* as an approach to delivering radiotherapy for patients with cancer of the anus and anal canal.

When dosimetric planning with standard 3-dimensional conformal radiotherapy predicts that the radiation dose to an adjacent organ would result in unacceptable normal tissue toxicity (see Policy Guidelines section), intensity-modulated radiotherapy may be considered *medically necessary* for the treatment of cancer of the abdomen and pelvis, including but not limited to:

- stomach (gastric);
- hepatobiliary tract;
- pancreas;
- rectal locations; or
- gynecologic tumors (including cervical, endometrial, and vulvar cancers).

Intensity-modulated radiotherapy would be considered *investigational* for all other uses in the abdomen and pelvis.

**POLICY GUIDELINES**

Table PG1 outlines radiation doses generally considered tolerance thresholds for normal structures in the abdomen and pelvis. Dosimetry plans may be reviewed to demonstrate that radiation by 3-dimensional conformal radiotherapy (3D-CRT) would exceed tolerance doses to structures at risk.

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5 (Gray)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TD 50/5 (Gray)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Complication End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Portion of Organ Involved</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1/3</td>
<td>2/3</td>
<td>3/3</td>
</tr>
<tr>
<td>Heart</td>
<td>60</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>Lung</td>
<td>45</td>
<td>30</td>
<td>17.5</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>50</td>
<td>50</td>
<td>47</td>
</tr>
<tr>
<td>Kidney</td>
<td>50</td>
<td>30</td>
<td>23</td>
</tr>
<tr>
<td>Liver</td>
<td>50</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>Stomach</td>
<td>60</td>
<td>55</td>
<td>50</td>
</tr>
<tr>
<td>Small intestine</td>
<td>50</td>
<td>NP</td>
<td>40</td>
</tr>
<tr>
<td>Femoral head</td>
<td>NP</td>
<td>NP</td>
<td>55</td>
</tr>
</tbody>
</table>

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NP: not provided; TD: tolerance dose.

a TD 5/5, the average dose that results in a 5% complication risk within 5 years.
b TD 50/5, the average dose that results in a 50% complication risk within 5 years.

For intensity-modulated radiotherapy (IMRT) to provide outcomes superior to 3D-CRT, there must be a clinically meaningful decrease in the radiation exposure to normal structures with IMRT compared with 3D-CRT. There is no standardized definition for a clinically meaningful decrease in radiation dose. In principle, a clinically meaningful decrease would signify a significant reduction in anticipated complications of radiation exposure. To document a clinically meaningful reduction in dose, dosimetry planning studies should demonstrate a significant decrease in the maximum dose of radiation delivered per unit of tissue, and/or a significant decrease in the volume of normal tissue exposed to potentially toxic radiation doses. While radiation tolerance dose levels for normal tissues are well-established, the decrease in the volume of tissue exposed that is needed to provide a clinically meaningful benefit has not been standardized. Therefore, precise parameters for a clinically meaningful decrease cannot be provided.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

In general, IMRT systems include intensity modulators which control, block, or filter the intensity of radiation; and RT planning systems which plan the radiation dose to be delivered.

A number of intensity modulators have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Intensity modulators include the Innocure Intensity Modulating Radiation Therapy Compensators (Innocure), cleared in 2006, and the decimal tissue compensator (Southeastern Radiation Products), cleared in 2004. FDA product code: IXI. Intensity modulators may be added to standard linear accelerators to deliver IMRT when used with proper treatment planning systems.

RT planning systems have also been cleared for marketing by FDA through the 510(k) process. They include the FOCUS Radiation Treatment Planning System (Computerized Medical Systems) in 2002, Prowess Panther™ (Prowess) in 2003, TiGRT (LinaTech) in 2009, and the RayDose (RaySearch Laboratories) in 2008, and the Eclipse Treatment Planning System (Varian Medical Systems) in 2017. FDA product code: MUJ.

Fully integrated IMRT systems also are available. These devices are customizable and support all stages of IMRT delivery, including planning, treatment delivery, and health record management. Varian Medical Systems has several 510(k) marketing clearances for high-energy linear accelerator systems that can be used to deliver precision RT such as IMRT. FDA product code: IYE.

RATIONALE

Summary of Evidence

For individuals who have GI tract cancers who receive IMRT, the evidence includes nonrandomized comparative studies and retrospective series. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. IMRT has been compared with 3D-CRT for the treatment of stomach, hepatobiliary, and pancreatic cancers. Evidence has been inconsistent with the outcome of survival, with some studies reporting increased survival among patients receiving IMRT compared with patients receiving 3D-CRT, and other studies reporting no difference between groups.
However, most studies found that patients receiving IMRT experienced significantly less GI toxicity compared with patients receiving 3D-CRT. The available comparative evidence, together with dosimetry studies of organs at risk, would suggest that IMRT decreases toxicity compared with 3D-CRT in patients who had GI cancers. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have gynecologic cancers who receive IMRT, the evidence includes 2 small randomized controlled trials and several nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. There is limited comparative evidence on survival outcomes following IMRT or 3D-CRT. However, results are generally consistent that IMRT reduces GI and genitourinary toxicity. Based on evidence with other cancers of the pelvis and abdomen that are proximate to organs at risk, it is expected that overall survival with IMRT would be at least as good as 3D-CRT, with a decrease in toxicity. A reduction in GI toxicity is likely to improve the quality of life in patients with gynecologic cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have anorectal cancer who receive IMRT, the evidence includes a small randomized controlled trial (N=20), nonrandomized comparative studies, and case series. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. Survival outcomes have not differed significantly between patients receiving IMRT and 3D-CRT. However, studies have found that patients receiving IMRT plus chemotherapy for the treatment of anal cancer experience fewer acute and late adverse events than patients receiving 3D-CRT plus chemotherapy, primarily in GI toxicity. A reduction in GI toxicity is likely to improve the quality of life in patients with anorectal cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Comprehensive Cancer Network Guidelines

Gastrointestinal Tract Cancers
The National Comprehensive Cancer Network (NCCN) guidelines for gastric cancer (v.2.2018) indicate that intensity-modulated radiotherapy (IMRT) "may be used in clinical settings where reduction in dose to organs at risk (e.g., heart, lungs, liver, kidneys, small bowel) is required, which cannot be achieved by 3-D techniques." In addition, target volumes need to be carefully defined and encompassed while taking into account variations in stomach filling and respiratory motion.

NCCN guidelines for hepatobiliary cancers (v.1.2018) state that "All tumors irrespective of the location may be amenable to radiation therapy (3D conformal radiation therapy, intensity-modulated radiation therapy [IMRT], or stereotactic body radiation therapy [SBRT])."

IMRT is mentioned as an option in NCCN guidelines for pancreatic adenocarcinoma (v.1.2018), stating that 3-dimensional conformal radiotherapy or IMRT with breath-hold or gating techniques can improve coverage with decreased dose to organs at risk. In addition, "studies have shown that the tolerability of radiation is largely dependent on PTV [planning target volume] size/ENI [elective nodal irradiation], types of concurrent systemic/targeted therapy, and whether conformal (3-D, IMRT, SBRT) vs. conventional radiation is used."

Gynecologic Cancers
For cervical cancer, NCCN guidelines (v.1.2018) indicate IMRT "may be helpful in minimizing the dose to the bowel and other critical structures in the post-hysterectomy setting and in treating the para-aortic
nodes when necessary,” such as “when high doses are required to treat gross disease in regional lymph nodes.” IMRT “should not be used as routine alternatives to brachytherapy for treatment of central disease in patients with an intact cervix.” The guidelines also mention that “very careful attention to detail and reproducibility (including consideration of target and normal tissue definitions, patient and internal organ motion, soft tissue deformation, and rigorous dosimetric and physics quality assurance) is required for proper delivery of IMRT and related highly conformal technologies.”

NCCN guidelines on uterine endometrial cancer (v.2.2018) state that radiotherapy for uterine neoplasms includes external-beam radiotherapy and/or brachytherapy, but that IMRT may be considered “for normal tissue sparing.”

NCCN guidelines on ovarian cancer (v.2.2018) do not mention IMRT.

Anorectal Cancers
NCCN guidelines for anal carcinoma (v.1.2018) state that IMRT “is preferred over 3D conformal RT [radiotherapy] in the treatment of anal carcinoma”; and that “Its use requires expertise and careful target design to avoid reduction in local control by so-called ‘marginal-miss’.”

NCCN guidelines on rectal cancer (v.1.2018) indicate that “… IMRT … should only be used in the setting of a clinical trial or in unique clinical situations such as reirradiation of previously treated patients with recurrent disease or unique anatomical situations.”

American College of Radiology
The American College of Radiology Appropriateness Criteria (2014) recommended that IMRT is usually appropriate to treat anal cancer if performed outside of a protocol setting but is still undergoing study. The College also noted the most appropriate radiation dose for anal cancer has not been determined and quality control and technical problems are considered challenging with IMRT (eg, in target volume contouring).

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

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POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 2012</td>
<td>New Policy</td>
<td>Policy updated with literature review, no new references added, reordered. Policy statement changed to IMRT may be considered medically necessary for all anal cancers (not limited to squamous cell carcinoma); IMRT may be medically necessary for treatment of tumors of abdomen and pelvis when dosimetric planning predicts the volume of small intestine receiving doses &gt; 45 Gy with standard 3-D conformal radiation would result in unacceptable risk of small intestine injury. Added statement that IMRT is considered investigational for all other uses in the abdomen and pelvis. Paragraph added to guidelines regarding toxic radiation dose to tissues and definition of a clinically significant decrease in radiation dose.</td>
</tr>
<tr>
<td>March 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature search. References 8, 13, 24-30 and 36-37 added. Policy statements unchanged</td>
</tr>
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<td>March 2015</td>
<td>Update Policy</td>
<td></td>
</tr>
<tr>
<td>September 2018</td>
<td>Update Policy</td>
<td>Policy updated with literature review through May 7, 2018; references 6-8, 12-13 and 23 added; references 19-26 and 33-40 updated; Policy statements unchanged</td>
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</table>

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